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APPLICATION NO.	FILING DATE	GROUP ART UNIT	FIL FEE REC'D	ATTORNEY DOCKET NO.
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ALLEN, M

18N2/0907

SWANSON & BRATSCHUN, L.L.C.
8400 EAST PRENTICE AVENUE
SUITE 200
ENGLEWOOD, COLORADO 80111

PAPER NUMBER	
1812	20

DATE MAILED: 09/07/95

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-26, 28-29, 31, 34-74 are pending in the application.
   Of the above, claims 1-25, 37-41, 56-74 are withdrawn from consideration.
2. ☒ Claims 27, 30, 32-33 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 26, 28-29, 31, 34-36, 42-55 are rejected.
5. ☐ Claims _____ are objected to.
6. ☒ Claims 1-26, 28-29 31, 34-74 are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☒ been received ☐ not been received per 35USC 371
    ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Applicant's election without traverse of Group III, claims 26-36 and 42-55, in Paper No. 18 is acknowledged.

Claims 1-25, 37-41, and 56-74 have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention. Election was made **without** traverse in Paper No. 18.

Claims 27, 30, 32, and 33 have been cancelled. As such, claims 26, 28-29, 31, 34-36, and 42-55 are under consideration by the Examiner.

If applicant desires priority under 35 U.S.C. § 120 based upon a parent application, specific reference to the parent application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. Status of the parent application (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "Patent No." should follow the filing date of the parent application. If a parent application has become abandoned, the expression "abandoned" should follow the filing date of the parent application.

The disclosure is objected to because of the following informalities: Sequences disclosed in the figures should be referenced by SEQ ID NO. in the brief description of the drawings.

Furthermore, it is noted that the precursor protein amino acid sequences do not appear to be present in the sequence listing.

It is noted that any additions or corrections to the sequence listing will require submission of a new CRF. A new sequence listing will need to be submitted to replace the present one in the specification. A statement that the content of the paper and

computer readable copies are the same and contain no new matter would also need to be submitted.

Appropriate correction is required.

Claims 26, 28-29, 31, 34-36, and 42-55 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to nucleic acid sequences encoding the GDNF amino acids sequences of Figures 13 and 19. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The specification broadly defines "glial derived neurotrophic factor" to include biological equivalents and alternative forms of the specific rat and human GDNF proteins set forth in Figures 13 and 19. (See pages 16-17 and 19-20.) Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable identification of any other nucleic acid sequences encoding a protein meeting the functional definition of a GDNF and it is deemed to constitute undue experimentation to determine them. The enablement of the claims can be viewed similarly to those in Ex parte Maizel, 27 USPQ2d 1662, 1665. The Board of Patent Appeals and Interferences held that claims drawn to DNA sequences encoding biologically equivalent proteins (i.e. DNA encoding proteins that do not have a defined amino acid sequence) are not enabled when the specification discloses a single specific DNA sequence known to the inventor having the biological limitations. The disclosure was held not to be commensurate in scope with the breadth of such claims because DNA sequences encoding biologically equivalent

proteins covers any DNA sequence encoding a protein which achieves the stated biological result. The disclosure is not commensurate in scope with the breadth of the claims.

In addition, the specification fails to fully characterize those amino acid sequences necessary for the biological activity of the protein. The specification does not describe those fragments of the disclosed sequences that would be expected to have activity. It would have been unpredictable to identify those fragments having activity in the absence of further guidance. Thus, for example, there does not appear to be any reason to expect that SEQ ID NO: 8 encodes an active protein. The specification does not describe how to use nucleic acid sequences that do not encode active proteins.

With respect to claim 36 parts (e) and (f), the specification does not appear to define what "dopaminergic activity" encompasses. The description in the specification would not permit one to contemplate those nucleic acid sequences that would have this activity as well as bind to an antibody or hybridize to a complementary sequence. These sequences are not deemed to be adequately described nor enabled. (See In re Deuel, 51 F3d 1552, 34 USPQ2d 1210 (Fed. Cir. 1995).) It is noted that the full length GDNF proteins of Figures 13 and 19 can cause mesencephalic neurons to increase uptake of dopamine. This activity is not synonymous with dopaminergic activity.

With respect to claim 44, the specification does not appear to describe what "conditions for amplification of the vector" encompass or what types of amplification are intended. "Amplification" to one of ordinary skill in the art could include

such diverse processes as PCR amplification and methotrexate amplification.

Claims 28, 31, and 35-36 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 is directed to a nucleic acid sequence encoding a mature human GDNF and recites "as set forth in Figure 19 (SEQ ID NO: 5)." Figure 19 depicts both the amino acid sequence and DNA sequence. It depicts both the mature and precursor amino acid sequence. SEQ ID NO: 5 is a particular DNA sequence for the precursor sequence. Thus, the claim is inconsistent and unclear as to whether the entire specific sequence of SEQ ID NO: 5 is being claimed, a portion thereof, or all degenerate sequences encoding a specific amino acid sequence of Figure 19.

Claims 31 and 35-36 are similarly confusing by citing both a Figure having DNA and amino acid sequences and SEQ ID NOS. In addition, it is noted that Figure 22 and SEQ ID NO: 8 provide only a small portion of the GDNF sequence and not the full precursor protein.

Claims 31 and 36 part (c) are additionally confusing in that they appear to claim two nucleic acid sequences (SEQ ID NOS: 5 and 8) simultaneously rather than in the alternative.

For example, applicant could make the claims unambiguous by amending approximately as follows:

"An isolated nucleic acid sequence encoding the mature human glial derived neurotrophic factor of SEQ ID NO: 6."

"An isolated nucleic acid sequence for mature human glial derived neurotrophic factor consisting of nucleotides 105 to 506 of SEQ ID NO: 5."

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26, 29, 34, 42-43, 50-54 are rejected under 35 U.S.C. § 102(b) as being anticipated by Monard et al. (EPO 233, 838).

Monard et al. discloses the human and rat DNA sequences for glia-derived neurite-promoting factor, GdNPF. The mature and precursor sequences are identified. The encoded protein can be produced recombinantly in E. coli or COS-7 cells. (See abstract, pages 6-9, 13, and 19.)

The specification broadly defines "glial derived neurotrophic factor" to encompass any protein identified in or obtained from glial cells and having neurotrophic activity. (See page 16, line 25.) Monard et al. discloses DNA sequences encoding GdNPF that meet the limitations of the claims as well as recombinant methods of production using vectors and host cells.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claim 44 is rejected under 35 U.S.C. § 103 as being unpatentable over Monard et al. in view of Wurm et al.

Monard et al. is applied as above. Monard et al. does not teach the step of amplification.

Wurm et al. teaches amplification and stability of plasmid sequences in CHO cells and the applications in recombinant production of proteins. (See page 159-161.)

Amplification of vectors would have been well known and routine to those of ordinary skill in the art as demonstrated by Wurm et al. Thus, it would have been obvious to perform an

amplification step when producing GdNPF in mammalian cells such as CHO cells. One would have been motivated to do so for the known advantages of amplification.

Claim 55 is rejected under 35 U.S.C. § 103 as being unpatentable over Monard et al. in view of Olson et al. (U.S. Patent No. 4,518,526).

Monard et al. is applied as above. Monard et al. does not teach the step of refolding the harvested protein.

Olson et al. teaches solubilizing refractile bodies and refolding the recombinant proteins contained therein. (See abstract, claims, column 1.)

Refolding of recombinant proteins would have been well known and routine to those of ordinary skill in the art as demonstrated by Olson et al. Thus, it would have been obvious to perform a refolding step when producing GdNPF in host cells such as E. coli. One would have been motivated to do so to improve the yield of biologically active protein.

Claims 28, 31, and 35-36 are allowable over the prior art of record. The prior art of record does not anticipate nor suggest the nucleic acid sequences disclosed in the named figures or SEQ ID NOS.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen, whose telephone number is (703) 308-0666. The examiner can

normally be reached on Monday-Thursday from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Garnette D. Draper, can be reached on (703) 308-4232. The most convenient FAX telephone number for Art Unit 1812 is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1800